DEVELOPMENT OF A HIGHLY EFFICIENT AND FLEXIBLE MEDIA SYSTEM FOR CHO FED-BATCH CULTURE

Yang Li, Upstream Process Development, Celgene Corporation, USA
yangli@celgene.com
Zhe Zhang, Upstream Process Development, Celgene Corporation, USA
Aaron Zheng, Upstream Process Development, Celgene Corporation, USA
Nicole Polombit, Upstream Process Development, Celgene Corporation, USA
Weiwei Hu, Upstream Process Development, Celgene Corporation, USA
Xiao-Ping Dai, Upstream Process Development, Celgene Corporation, USA

The production of protein-based biotherapeutics through mammalian cell culture requires in-depth understanding of medium composition, which delivers adequate and balanced nutrients to meet cell growth, metabolism, and protein production requirements. Commercially available media developed for broad applications intend to cover a range of host cell systems and bioprocesses, and therefore are not optimized enough to meet the specific demand of high performance and versatility. Here, we present a systematic approach towards developing an in house fed-batch medium system using a CHO cell line for manufacturing biologics products.

In this work, a chemically defined medium formulation was developed through a multi-layer approach utilizing a combination of high-throughput well plate, shake flask, and fully controlled AMBR15 bioreactor system. OFAT screening and DOE studies combined with multivariate analysis were conducted to understand the impact of individual medium component and interactions on defined process parameters. The basal medium was developed under six months after rigorous optimization to achieve peak viable cell density (VCD) higher than 15E6 cells/mL using cell lines that secret a wide range of products including mAbs, fusion proteins, and bispecific antibodies. Evaluation comparing to commercial media demonstrated superior peak VCD, sustained viability and productivity from our internally-developed basal medium.

To support high performing fed-batch culture, an in-house feed medium was developed based on nutrient consumption analysis. A high peak VCD (> 30E6 cells/mL) was achieved using selected cell lines with prolonged viability in a 14-day fed-batch culture. The titers were in the range of 3 – 6 g/L. The in house medium system developed offers great flexibility towards tuning clone-dependent cell growth and metabolic profiles to maximize cell culture performance and productivity due to the systematic knowledge gained in the development. This system is being further developed to incorporate the aspect of product quality attributes such as N-glycan profile and charge variants. The establishment of such a systematic media toolbox can be utilized to make predictive modeling of key process parameters and quality attributes to accelerate the development of highly efficient and productive bioprocesses.